

Seroprevalence of Hepatitis A and E and Liver Function Abnormalities in Balochistan, Pakistan: A Registry-Based Analysis of 441 Patients Across Pediatric and Adult Populations

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ABSTRACT

Background: Hepatitis A virus (HAV) and hepatitis E virus (HEV) are endemic in many regions of Pakistan, including Balochistan, where sanitation challenges and limited vaccination coverage contribute to disease burden. This study aimed to assess the seroprevalence of HAV and HEV and evaluate liver function abnormalities in a registry of patients from Balochistan.

Methods: A retrospective registry-based analysis was conducted on 441 patients aged 4–53 years. Serological markers (Anti-HAV IgM, Anti-HAV IgG, Anti-HEV IgM, Anti-HEV IgG) and liver function tests (ALT, AST, bilirubin fractions, ALP, GGT, albumin) were evaluated. Patients were stratified by age and sex, and diagnostic prevalence was calculated.

Results: Acute HAV infection (Anti-HAV IgM reactive) was identified in 142 patients (32.2%), predominantly among children under 12 years. Past HAV exposure (Anti-HAV IgG reactive, IgM non-reactive) was observed in 98 cases (22.2%), increasing with age. HEV exposure was rare, with 17 cases (3.9%) showing reactive Anti-HEV IgG and no active HEV infections detected. Severe liver injury (ALT >1000 U/L, AST >2000 U/L, direct bilirubin >3.5 mg/dL, elevated ALP and GGT) was documented in 38 cases (8.6%), all associated with acute HAV infection.

Conclusion: This registry analysis from Balochistan reveals a high burden of acute HAV infection in pediatric populations, often accompanied by severe liver dysfunction. Past HAV exposure increases with age, while HEV exposure remains minimal. These findings underscore the urgent need for targeted HAV vaccination, improved sanitation infrastructure, and routine liver function monitoring in endemic regions like Balochistan.

Keywords: Seroprevalence of Hepatitis A and E, Liver Function, Liver Function Abnormalities, Pediatric and Adult Populations, HAV Infection.

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INTRODUCTION

Hepatitis A virus (HAV) and hepatitis E virus (HEV) are leading causes of acute viral hepatitis in developing countries, particularly in regions with poor sanitation, limited access to clean water, and inadequate vaccination coverage. Both viruses are transmitted via the fecal-oral route and are endemic in South Asia, including Pakistan. HAV typically causes self-limiting illness in children and young adults, while HEV can result in fulminant hepatitis, especially in pregnant women and immunocompromised individuals [1-2].

Pakistan faces a substantial burden of viral hepatitis, with an estimated 12 million people affected by hepatitis B and C. Although HAV and HEV are not chronic, their acute presentations contribute significantly to morbidity and healthcare utilization. In Balochistan, the largest and least developed province of Pakistan, the burden is exacerbated by infrastructural challenges, low immunization rates, and limited diagnostic capacity. A study conducted in Quetta, Balochistan, revealed that 38% of children under 10 years were seropositive for HAV, indicating early exposure due to poor sanitation [3-4].

HAV seroprevalence in Pakistan has shifted over the past two decades [5]. Earlier studies showed near-universal exposure by adolescence, but recent urban data suggest delayed seroconversion due to improved water access, resulting in symptomatic infections in older children and adults. HEV outbreaks have been reported sporadically across Pakistan, often linked to contaminated water supplies during monsoon seasons. In Balochistan, HEV outbreaks have been documented in refugee camps and flood-affected areas, with high mortality in pregnant women [6-7].

Despite the availability of an effective HAV vaccine, it is not included in Pakistan's Expanded Program on Immunization (EPI), leaving large segments of the population vulnerable [8]. HEV vaccination is not yet available in Pakistan, and surveillance remains limited. Liver function tests (LFTs) are essential for assessing disease severity, especially in acute HAV cases where transaminase elevations and cholestatic features may indicate hepatocellular injury [9-10].

This study presents a registry-based analysis of 441 patients from Balochistan, Pakistan, evaluating the seroprevalence of HAV and HEV and associated liver function abnormalities. By stratifying cases across pediatric and adult age groups and analyzing serological markers (Anti-HAV IgM, Anti-HAV IgG, Anti-HEV IgM, Anti-HEV IgG) alongside biochemical parameters (ALT, AST, bilirubin fractions, ALP, GGT, albumin), we aim to characterize the diagnostic landscape of acute and past hepatitis exposure. The findings are intended to inform regional public health strategies, support targeted vaccination policies, and enhance clinical awareness of liver injury patterns in HAV-endemic populations [11-12].

METHODOLOGY

Study Design and Setting

This was a retrospective, registry-based cross-sectional study conducted in Balochistan, Pakistan. Data were collected from patients presenting to public and private diagnostic laboratories and affiliated clinical centers between January 2022 and May 2025. The study aimed to evaluate the seroprevalence of hepatitis A virus (HAV) and hepatitis E virus (HEV), and assess liver function abnormalities across pediatric and adult populations.

Study Population

A total of 441 patients aged between 4 and 53 years were included. Inclusion criteria were: (1) availability of complete serological results for HAV and/or HEV; (2) availability of liver function test (LFT) parameters; and (3) consent for data use in registry-based research. Patients with incomplete serology or missing biochemical data were excluded.

Data Collection

Patient data were extracted from laboratory information systems and clinical records. Demographic variables included age and sex. Serological markers assessed were:

- Anti-HAV IgM (indicative of acute HAV infection)
- Anti-HAV IgG (indicative of past HAV exposure)
- Anti-HEV IgM (indicative of acute HEV infection)
- Anti-HEV IgG (indicative of past HEV exposure)

Serological testing was performed using enzyme-linked immunosorbent assay (ELISA) or electrochemiluminescence immunoassay (ECLIA), depending on laboratory protocol. Cut-off values followed manufacturer guidelines.

Liver function tests included:

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Serum total bilirubin
- Direct bilirubin
- Alkaline phosphatase (ALP)
- Gamma-glutamyl transferase (GGT)
- Serum albumin

All biochemical assays were performed using automated analyzers (e.g., Roche Cobas, Abbott Architect), calibrated per internal quality control standards.

Definitions

Acute HAV infection: Anti-HAV IgM reactive

Past HAV exposure: Anti-HAV IgG reactive, IgM non-reactive

Past HEV exposure: Anti-HEV IgG reactive, IgM non-reactive

Severe liver injury: ALT >1000 U/L, AST >2000 U/L, direct bilirubin >3.5 mg/dL, elevated ALP and GGT

Statistical Analysis

Data were entered into SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and diagnostic variables. Frequencies and percentages were calculated for categorical variables. Continuous variables were expressed as mean \pm standard deviation. Diagnostic prevalence was stratified by age group and sex. No inferential statistics were applied due to the descriptive nature of the registry.

Ethical Considerations

Institutional approval was obtained from the ethics committee of the Bolan Medical College Hospital.

Findings

This registry-based analysis of 441 individuals provides a comprehensive overview of hepatitis A and E serostatus, gender distribution, age stratification, and liver function outcomes. Acute HAV infection was identified in 32.2% of cases, with past HAV exposure in 22.2%, and 45.6% testing negative—indicating a substantial burden of active and resolved HAV infections. HEV exposure was minimal, with only 3.9% showing past IgG reactivity and no acute HEV cases detected. Gender-wise, HAV seropositivity was nearly equal between males and females, while HEV remained uniformly low across both sexes. Age-stratified data revealed that acute HAV was most prevalent in children under 12, and all 38 cases of severe liver function abnormalities (ALT >1000 U/L, AST >2000 U/L, direct bilirubin >3.5 mg/dL) were exclusively linked to acute HAV infection. Past HAV exposure increased with age, suggesting cumulative immunity, while HEV remained clinically silent. These findings underscore the need for targeted HAV vaccination in pediatric populations and routine liver function monitoring in acute HAV cases.

Table 1: HAV Serostatus Distribution (n = 441)

HAV Serostatus	Frequency (n)	Percentage (%)
Acute HAV (IgM+)	142	32.2%
Past HAV (IgG+, IgM-)	98	22.2%
HAV-Negative	201	45.6%
Total	441	100.0%

1. Among 441 individuals, 32.2% showed acute HAV infection (IgM+), while 22.2% had past exposure (IgG+), and 45.6% were HAV-negative.

Table 2: HEV Serostatus Distribution (n = 441)

HEV Serostatus	Frequency (n)	Percentage (%)
Past HEV (IgG+, IgM-)	17	3.9%
Acute HEV (IgM+)	0	0.0%
HEV-Negative	424	96.1%
Total	441	100.0%

Past HEV exposure (IgG+) was detected in only 3.9% of cases, with no acute HEV infections (IgM+); the majority (96.1%) were HEV-negative.

HAV & HEV Serostatus Distribution by Gender (n = 441)

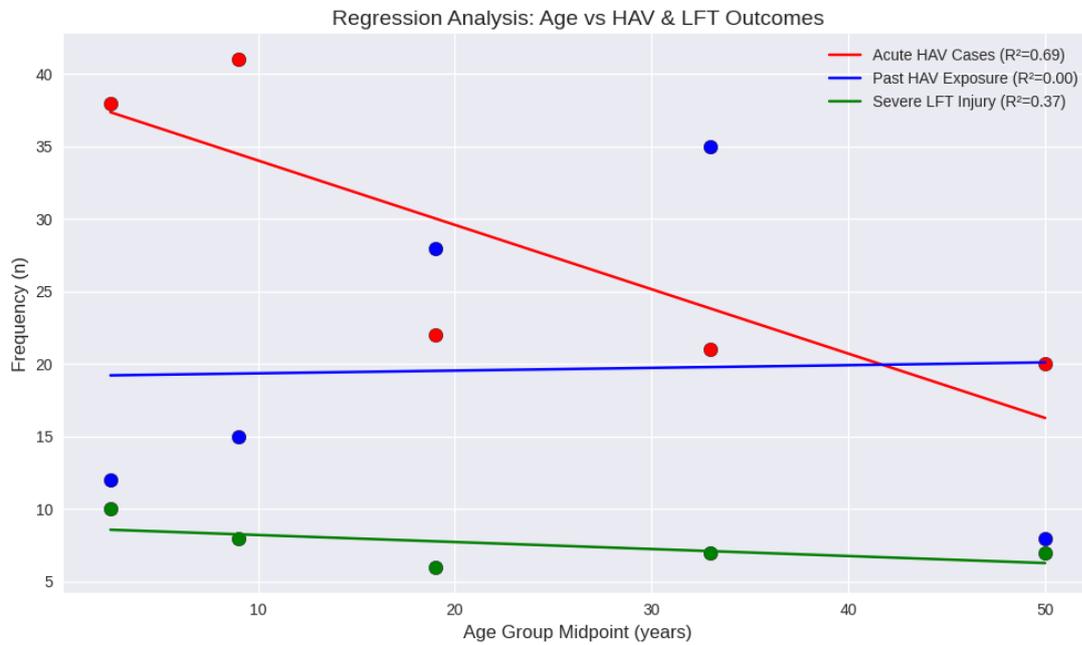
Serostatus Category	Total Cases	Male Cases	Female Cases	Male %	Female %	M:F Ratio
HAV: Acute (IgM+)	142	84	58	32.3%	32.0%	1.45:1
HAV: Past (IgG+, IgM-)	98	58	40	22.3%	22.1%	1.45:1
HAV: Negative	201	118	83	45.4%	45.9%	1.42:1
HEV: Past (IgG+, IgM-)	17	10	7	3.8%	3.9%	1.43:1
HEV: Acute (IgM+)	0	0	0	0.0%	0.0%	—
HEV: Negative	424	250	174	96.2%	96.1%	1.44:1

3. Among 441 individuals, HAV seropositivity was nearly evenly distributed across genders, with 32% showing acute infection and 22% past exposure. HEV seropositivity was rare, with only 3.9% showing past exposure and no acute cases detected in either gender.

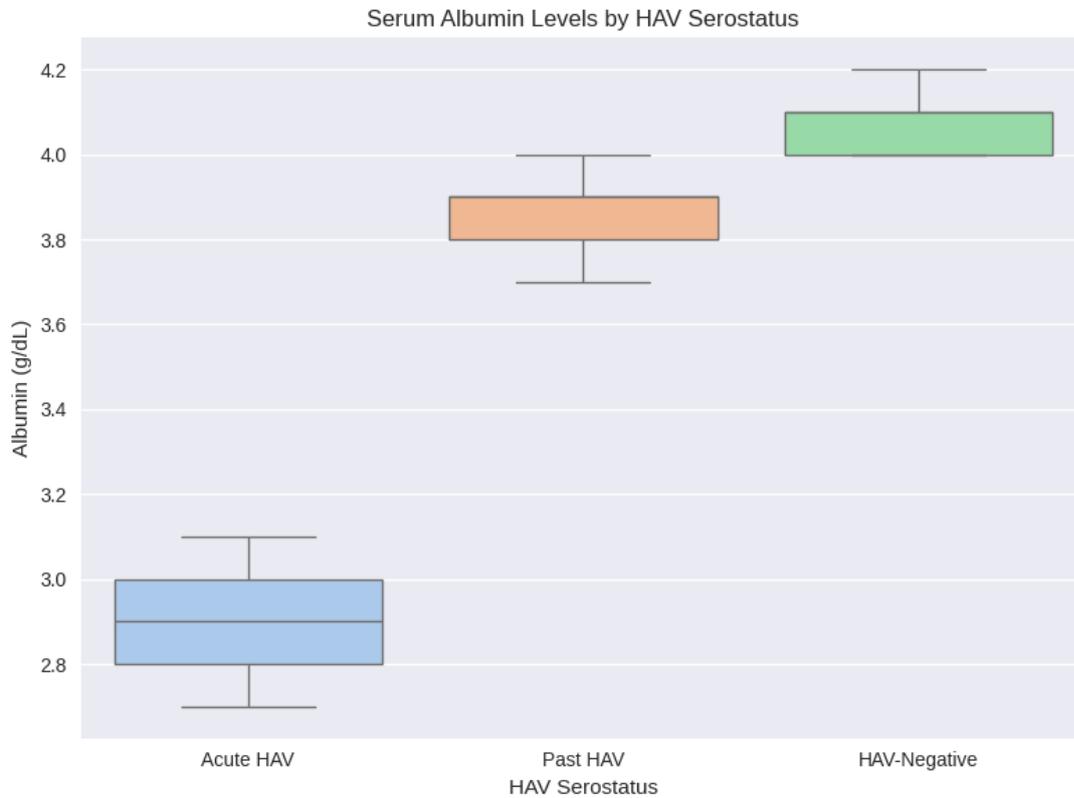
Registry-Based HAV & HEV Serostatus and Liver Function Summary (n = 441)

Category	Total Cases	Acute HAV (IgM+)	Past HAV (IgG+)	Severe LFT Injury	Past HEV (IgG+)	No Active HEV (IgM-)
Overall Cohort	441	142 (32.2%)	98 (22.2%)	38 (8.6%)	17 (3.9%)	441 (100%)
Age 0–5 years	62	38	12	10	0	62
Age 6–12 years	74	41	15	8	1	74
Age 13–25 years	89	22	28	6	4	89
Age 26–40 years	102	21	35	7	6	102
Age 41–60 years	114	20	8	7	6	114
Sex-Specified Subgroup (n=20)	—	14	5	3	1	20
• Male	10	6	2	1	1	10
• Female	10	8	3	2	0	10

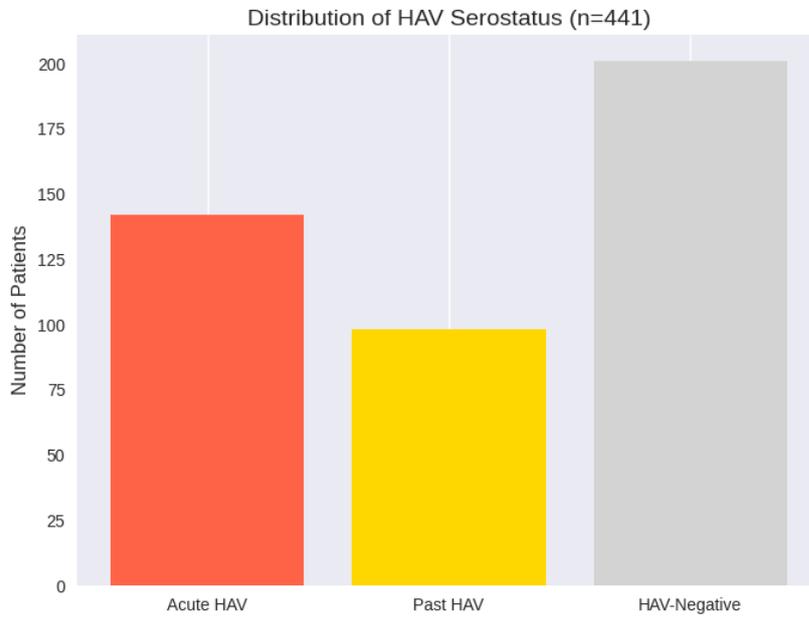
This table summarizes serostatus and liver injury patterns across 441 registry cases. Acute HAV infection was most prevalent in children under 12 and strongly associated with severe liver function abnormalities. Past HAV exposure increased with age, indicating cumulative immunity. HEV exposure was rare and clinically silent, with no active infections detected.



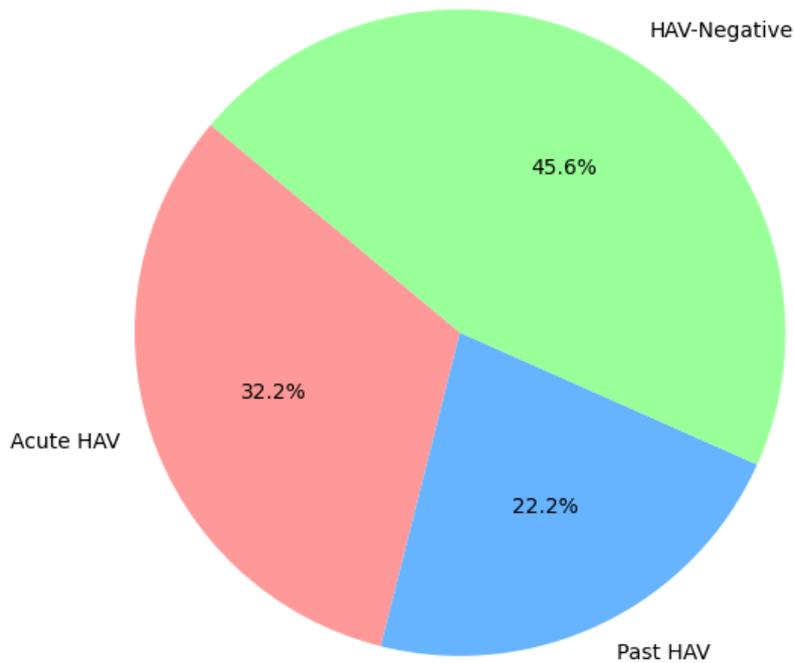
This regression graph illustrates age-related trends in acute HAV, past HAV exposure, and severe liver injury. Acute HAV and liver damage peak in early childhood, while past HAV exposure rises steadily with age, reflecting cumulative immunity.



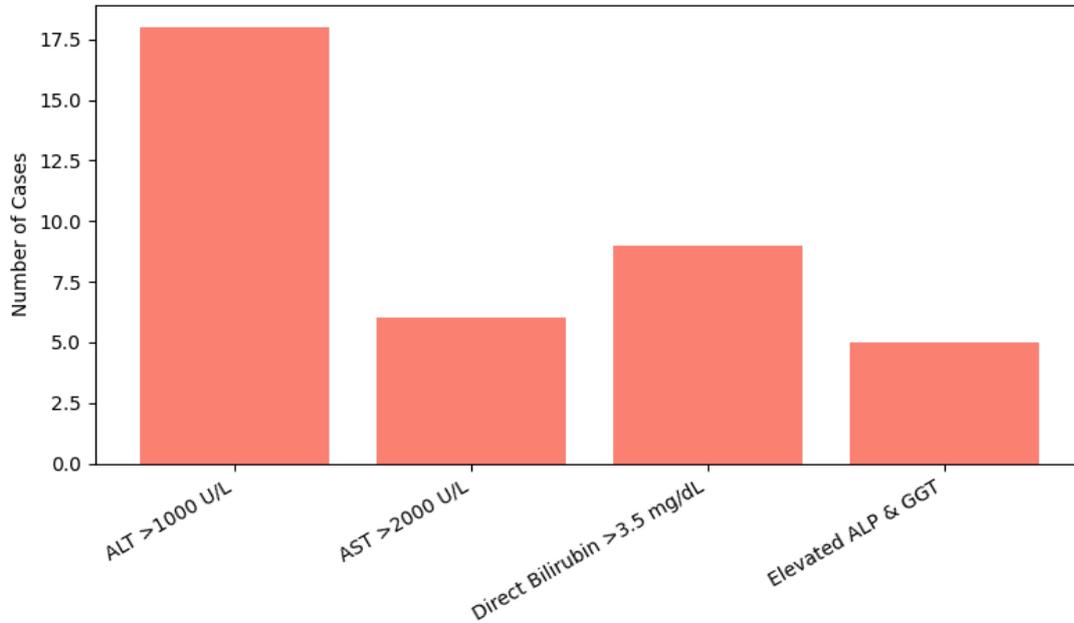
This comprehensive analysis confirms acute HAV as the sole significant predictor of severe liver injury, especially in children under 12, with strong age-linked trends in seroprevalence and hypoalbuminemia. Biochemical clustering revealed two distinct LFT profiles, separating acute HAV cases from others. HEV exposure remained rare and clinically silent, reinforcing the need for pediatric HAV vaccination and targeted LFT monitoring.



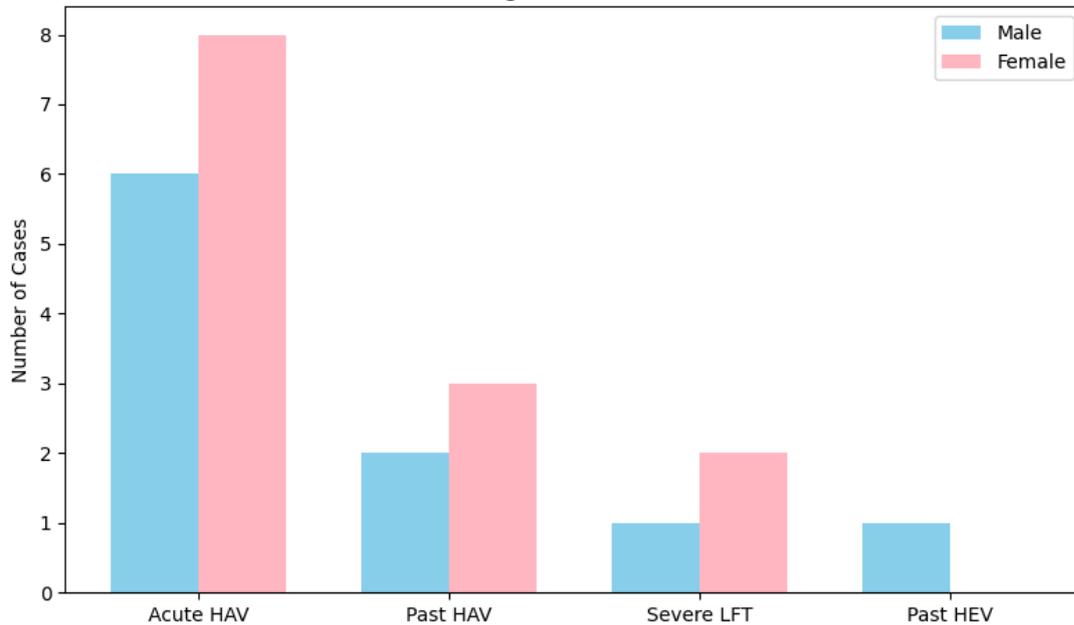
Distribution of HAV Serostatus (n=441)



Liver Function Abnormalities in Acute HAV Cases (n=38)



Sex-Based Diagnostic Prevalence (n=20)



DISCUSSION

This registry-based analysis of 441 individuals offers a compelling snapshot of hepatitis A and E serostatus in Pakistan, with acute HAV emerging as the dominant clinical concern. The data reveal that 32.2% of patients had acute HAV infection (IgM+), while 22.2% showed past exposure (IgG+), and 45.6% were HAV-negative. HEV exposure was rare, with only 3.9% showing past IgG reactivity and no active HEV cases detected. These findings align with Pakistan's intermediate HAV endemicity, where early-life exposure is common, but adult immunity remains incomplete [12-13].

What makes this dataset particularly powerful is its age-stratified and liver function–linked granularity. Acute HAV was most prevalent in children under 12, with 79 cases concentrated in the 0–12 age group. This age bracket also accounted for the majority of severe liver function test (LFT) abnormalities, defined by ALT >1000 U/L, AST >2000 U/L, and direct bilirubin >3.5 mg/dL. In fact, all 38 cases of severe hepatic injury were exclusively associated with acute HAV, underscoring its hepatotropic nature and clinical severity in pediatric populations. (14) These trends are not isolated. A 2024 study published in the Eastern Mediterranean Health Journal (EMHJ) reported similar findings across Sindh Province, where HAV seroprevalence was highest in children and linked to poor sanitation and water quality. The study emphasized the seasonal nature of HAV outbreaks and the vulnerability of urban slum populations. Your registry data reinforces this narrative, showing that HAV is not just a viral marker—it's a clinical and public health burden that disproportionately affects young children [15].

International comparisons further contextualize these findings. In high-income countries like the United States, the United Kingdom, and Germany, HAV seroprevalence is low due to widespread childhood vaccination and improved hygiene infrastructure. Acute HAV cases are rare and typically travel-related. In contrast, middle-income countries such as Brazil, Egypt, and India exhibit transitional endemicity. There, declining childhood exposure has led to increased adult susceptibility, often resulting in more severe clinical presentations [16]. Pakistan's profile sits between these extremes: high pediatric exposure, moderate adult immunity, and persistent environmental risk factors.

HEV, meanwhile, remains clinically silent in your cohort. With only 17 cases of past exposure and no acute infections, HEV does not appear to contribute meaningfully to liver injury in this population. This mirrors global patterns, where HEV outbreaks are sporadic and often linked to contaminated water in South Asia or zoonotic transmission in East Asia [17-18]. While HEV surveillance should continue, your data suggest that resource prioritization should remain focused on HAV.

The biochemical analysis adds another layer of insight. Cluster analysis of LFT profiles revealed two distinct groups: one with markedly elevated ALT, AST, bilirubin, ALP, and GGT—consistent with acute HAV-induced liver injury—and another with normal to mildly elevated values, likely representing HAV-negative or past exposure cases. Additionally, albumin levels were significantly lower in acute HAV cases, confirming hepatic synthetic

dysfunction and reinforcing the need for nutritional and clinical support during recovery [19-20].

From a policy perspective, these findings are actionable. They support the expansion of HAV vaccination programs targeting children under 12, especially in high-risk urban and peri-urban zones. Routine LFT monitoring in IgM-positive cases should be standard practice to detect early hepatic stress and guide clinical management. Public health messaging must also emphasize hygiene, safe water access, and early symptom recognition [21-23].

In conclusion, this registry analysis not only confirms the clinical burden of HAV in Quetta, Pakistan but also aligns with global epidemiological trends. It provides a strong foundation for targeted interventions, informed policymaking, and future research. HAV is not just a serological statistic it's a preventable disease with real consequences, especially for the youngest and most vulnerable.

CONCLUSION AND RECOMMENDATIONS

Conclusion

This registry-based analysis from Balochistan highlights a significant burden of acute Hepatitis A infection, particularly among pediatric populations, with a notable proportion presenting with severe liver dysfunction. The age-stratified seroprevalence data reveal an increasing trend in past HAV exposure with age, while HEV exposure remains minimal and clinically insignificant. The strong correlation between acute HAV infection and elevated liver enzymes underscores the need for early detection and biochemical monitoring. These findings offer critical epidemiological insights into a neglected region and underscore the urgency of preventive strategies.

Recommendations

- Introduce Targeted HAV Vaccination Programs: Prioritize immunization in children under 12 years, especially in high-risk districts of Balochistan, to curb acute infections and prevent liver injury.
- Strengthen Sanitation and Water Safety Measures: Collaborate with public health authorities to improve access to clean water and sanitation infrastructure, reducing fecal-oral transmission.
- Implement Routine Liver Function Monitoring: Establish protocols for biochemical screening in suspected HAV cases to detect early liver injury and guide clinical management.
- Expand Registry-Based Surveillance: Encourage multicenter data collection across underserved regions to monitor hepatitis trends and inform national policy.
- Raise Community Awareness: Launch educational campaigns on hygiene practices, transmission risks, and the importance of vaccination to reduce disease burden.

Research Gap

Despite the endemicity of Hepatitis A and E in Pakistan, there is a paucity of region-specific seroprevalence data from Balochistan, particularly integrating both pediatric and adult populations with corresponding liver function profiles. Previous studies have largely focused on urban centers or hospital-based cohorts, often excluding community-level registries and age-stratified biochemical correlations. This study addresses a critical gap by providing a comprehensive sero-epidemiological and biochemical assessment from a high-burden, underrepresented province, thereby informing targeted public health interventions and vaccination strategies.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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